An Integrated MRI and MRS Approach to Evaluation of Multiple Sclerosis with Cognitive Impairment

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Abstract. Magnetic resonance imaging and spectroscopy (MRI/MRS) plays a unique role in multiple sclerosis (MS) evaluation, because of its ability to provide both high image contrast and significant chemical change among brain tissues. The image contrast renders the possibility of quantifying the tissue volumetric and texture variations, e.g., cerebral atrophy and progressing speed, reflecting the ongoing destructive pathologic processes. Any chemical change reflects an early sign of pathological alteration, e.g., decreased N-acetyl aspartate (NAA) in lesions and normal appearing white matter, related to axonal damage or dysfunction. Both MRI and MRS encounter partial volume (PV) effect, which compromises the quantitative capability, especially for MRS. This work aims to develop a statistical framework to segment the tissue mixtures inside each image element, eliminating theoretically the PV effect, and apply the framework to the evaluation of MS with cognitive impairment. The quantitative measures from MRI/MRS neuroimaging are strongly correlated with the qualitative neuropsychological scores of Brief Repeatable Battery (BRB) test on cognitive impairment, demonstrating the usefulness of the PV image segmentation framework in this clinically significant problem.

1 Introduction

Multiple Sclerosis (MS) is the most common inflammatory demyelinating disease of central nervous system (CNS), characterized by repeated cycles of white matter

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(WM) damage, recovery, and injury. More than half of the MS patients develop cognitive dysfunction. The deficits often manifest in early adulthood and can profoundly disrupt occupational and social functioning. The domains most commonly disturbed are learning/recent memory, attention/information processing speed, verbal fluency, executive functions, and visuospatial skills. In this study we related neuropsychological performance to neuroimaging measures of cerebral injury in a group of subjects selected for cognitive impairment.

Volumetric analyses by magnetic resonance imaging (MRI) have shown that MS patients have significant cerebral atrophy (CA), progressing faster, reflecting the ongoing destructive pathologic processes [2, 7]. Cerebral atrophy has been shown to correlate with a variety of cognitive functions, including those functions most commonly disturbed. For example, correlations have been demonstrated for overall intellectual functioning, learning/recent memory, attention/information processing speed, and executive functions, though results for verbal fluency specifically have been somewhat inconsistent.

Studies of MS by ^{1}H magnetic resonance spectroscopy (MRS) have shown decreased levels of N-acetyl aspartate (NAA) in lesions and normal appearing WM (NAWM), related to axonal damage or dysfunction [1, 3, 6]. Decrease in NAA, or ratios of NAA over creatine (Cr) (NAA/Cr), NAA over choline compounds (NAA/Cho), are associated with more advanced disease and associated with level of disability. Two preliminary studies indicate that NAA levels may relate to cognitive variables as well, but further research is necessary to assess it as a neurobiological marker of cognitive impairment.

Although ^{1}H MRS has provided quantitative information about major pathologic aspects, it doesn't enable us to obtain information on specific brain tissues.

On the other hand, volumetric MRI analysis has provided morphological processes of brain tissues, but it doesn't enable us to obtain pathologic information underline the morphological processes.

The goal of this study is to map MR spectroscopy of interested chemical compounds onto their corresponding cerebral tissues and to establish an effective means to explore the complementary information between these two MR neural measures.

2 Methods

2.1 Theory

In the use of both MRI and MRS for quantitative analyses, a major challenge is associated with the partial volume (PV) effect, especially for MRS (because of its extremely low resolution at a cubic voxel size of 10 mm, while MRI can offer a resolution at 1 mm level). A theoretical solution to eliminate the PV effect is by the use of an image segmentation algorithm which is capable to quantify the tissue mixtures or percentages inside each image voxel. We have proposed an algorithm [4] and further developed it to segment the multi-spectral MR images in this work.

By acquiring the patient data within a same session of a short time period, we expect both MRI and MRS data are registered spatially. In other words, we have obtained the tissue fractions within each MRS voxel (of 10 mm side size) from the segmented tissue mixtures inside each MRI voxel (of 1 mm side size) [5].

The metabolite changes of the chemical compounds inside the cerebral tissues, measured by ^{1}H MRS, can be mapped onto the image voxels for correlation studies by the following formula

$$\text{NAA} = w\ \text{WM} + g\ \text{GM} + s\ \text{Lesion} \quad (1)$$

where we have assumed that WM has a weight factor of w contributing to the NAA measure, grey matter (GM) with a factor of g, and cerebral spinal fluid (CSF) with a factor of $c = 0$ and lesion with a factor of s. The complementary information between MRI and MRS leads to quantitative measures on both spatial and temporal correlations. Because both MRI and MRS images are spatially registered, a correlation between atrophy and NAA can be performed globally and locally across the field-of-view (FOV).

2.2 Data Acquisition

Multi-voxel ^{1}H MRS data were acquired with a 1.5T Phillips scanner with a PRESS sequence, TE = 135 ms, TR = 1500 ms, 16 cm FOV, 2D phase encoding (16x16), and 2 scan averages. The slice of interest with 2 cm thickness was taken through the posterior and anterior aspects of the corpus callosum. For each MRS voxel (1x1x2 cm^3), three peaks of *N*-acetyl aspartate compounds (or NAA), choline compounds (or Cho), and total creatine (or Cr) were digitized. Then the output of the MRS data is an image and each voxel contains the three digital values. From the three values in each MRS voxel, a ratio of NAA over Cho or NAA over Cr was computed for a relative measure of NAA level.

Multi-spectral (T1, T2, and FLAIR) MR images were acquired by the same scanner in the same session with voxel size of 0.9x0.9x1.5 mm^3 on an image slice of 256x256 array. To cover the whole brain space, more than one hundred image slices are usually generated for each T1, T2 or FLAIR scan. The eight corners' coordinates of the MRS image array were recorded within the MRI image array. The three multi-spectral T1, T2, and FLAIR images, as well as the MRS image are assumed registered spatially because all the data were acquired in the same session while the patient was lying on the scanner couch.

In addition, each MS patient underwent a modified version of the neuropsychological scores of Brief Repeatable Battery (BRB) test on cognitive functions.

3 Results

Participants were 38 individuals (20-55 years old) with relapsing remitting (60.5%) and secondary progressive (39.5%) MS. Each patient underwent the MRI/MRS data acquisition session and followed by a modified Brief Repeatable Battery (BRB) of neuropsychological tests. Figure 1 shows an example of the segmentation of multi-spectral MR images of a patient. Figure 2 shows an example of MRS data acquisition.

Figure 3 shows an example of mapping the central 8x8 MRS voxels onto the segmented MRI array of seven slices. From the segmented tissue mixture distributions in Figure 1 and the mapped NAA distribution in Figure 3, a correlation between atrophy and NAA can be performed globally and locally across the FOV. In the following, a series correlation studies are presented with extension to include BRB neuropsychological tests.

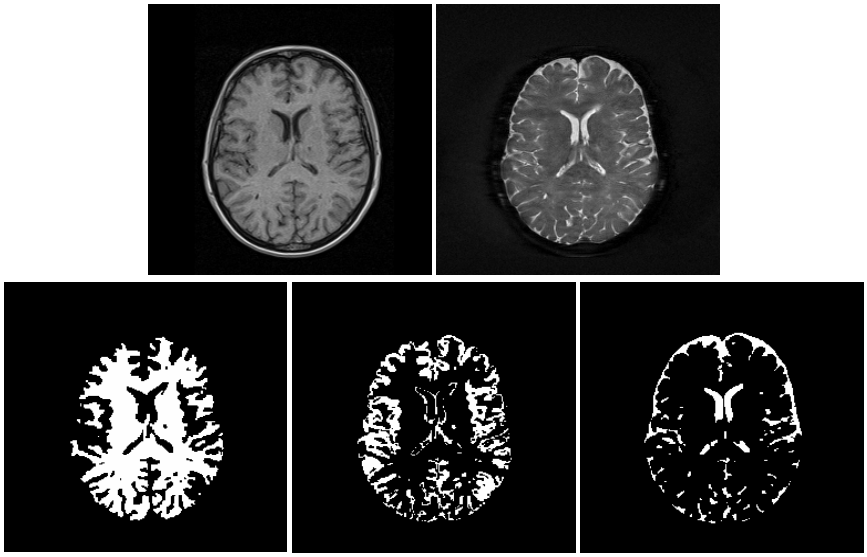

Fig. 1. Top left is a T1 image slice and top right is a T2 image slice at the same axial location. Bottom from left to right shows the segmented WM, GM, and CSF.

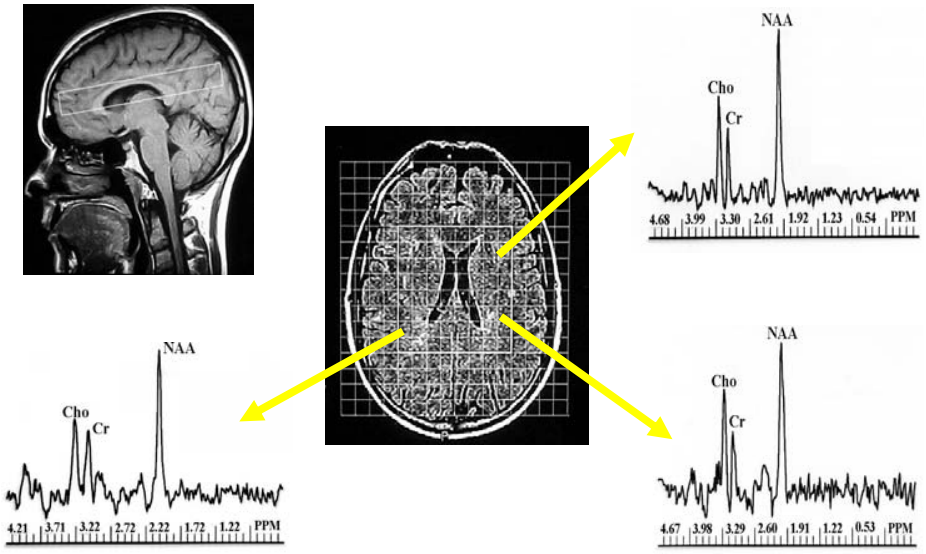

Fig. 2. Top left indicates the location of the MRS image volume taken through the posterior and anterior aspects of the corpus callosum. The middle shows a FLAIR image slice where the MRS voxel array was highlighted. Three MR spectra from three MRS voxels respectively are displayed.

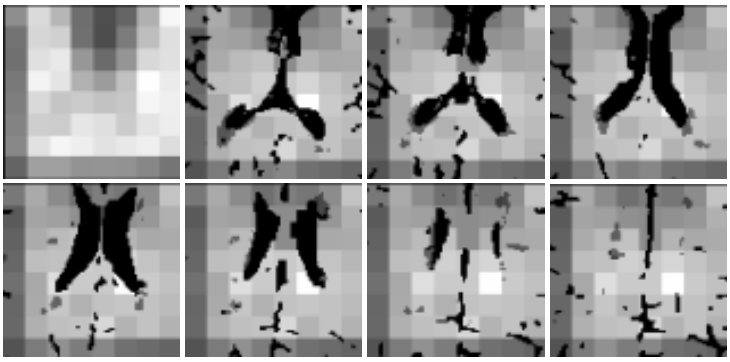

Fig. 3. A demonstration of mapping spectroscopic voxels (top left) to segmented image voxels, resulting in more accurate measure on both spatial and temporal correlations

3.1 Global Correlation – MRS and MRI

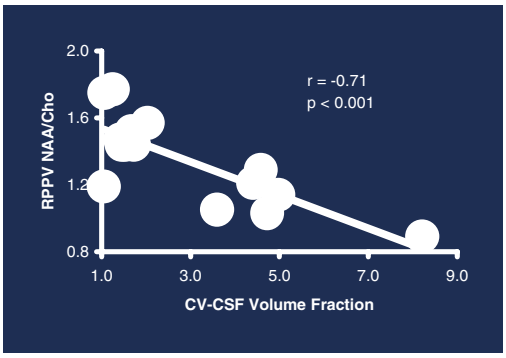

Fig. 4. Significant inverse relationship between NAA/Cho of right posterior periventricular (RPPV) and central ventricular (CV)-CSF volume fraction

3.2 Global Correlation – MRI and BRB

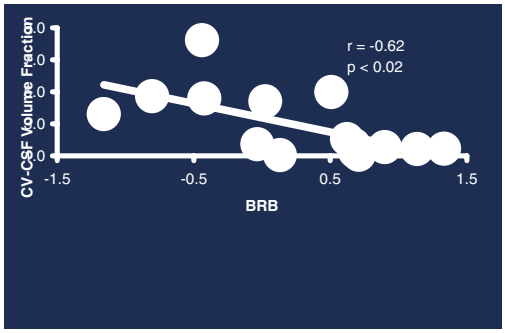

Fig. 5. Significant inverse relationship between central ventricular CV-CSF volume fraction and BRB scores

3.3 Global Correlation – MRS and BRB_{Cho}

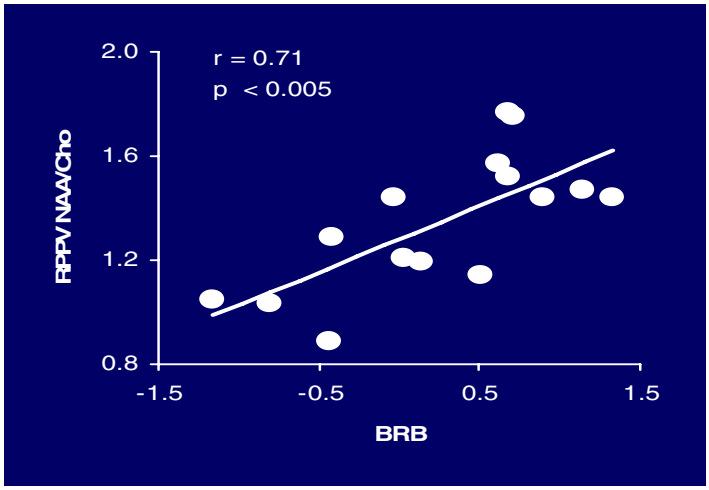

Fig. 6. Significant positive correlation between right posterior periventricular RPPV NAA/Cho and BRB scores

3.4 Global Correlation – MRS and BRB_{Cr}

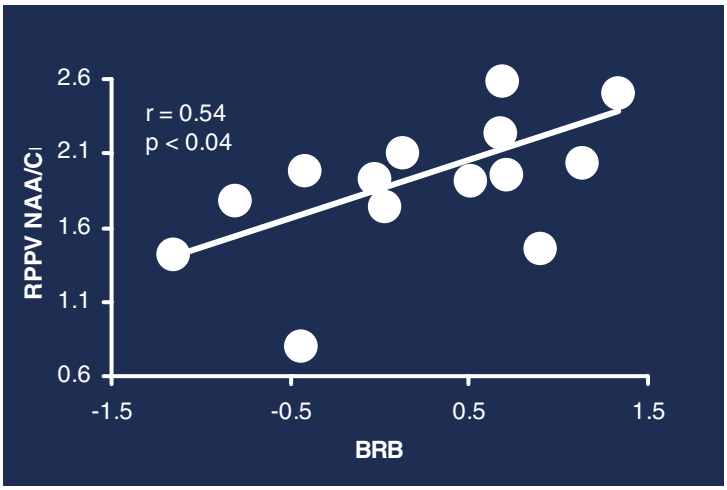

Fig. 7. Significant positive correlation between right posterior periventricular RPPV NAA/Cr and BRB scores

3.5 Local Correlation Study in WM_{Cho}

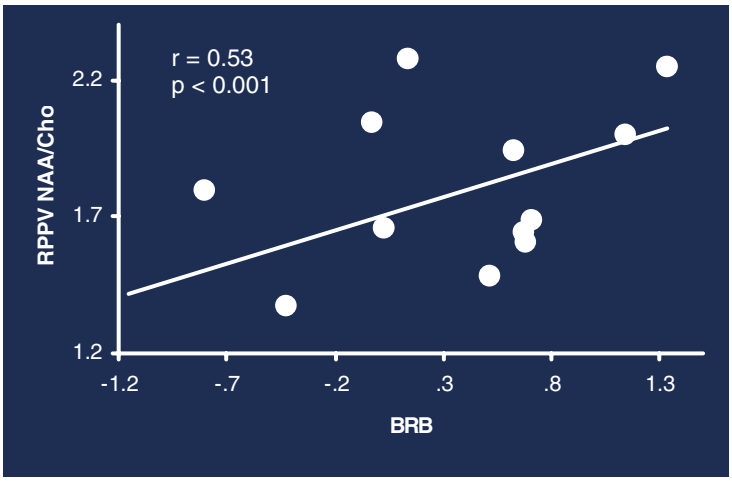

Fig. 8. A positive correlation between right posterior periventricular RPPV NAA/Cho and BRB scores in WM

3.6 Local Correlation Study in WM_{Cr}

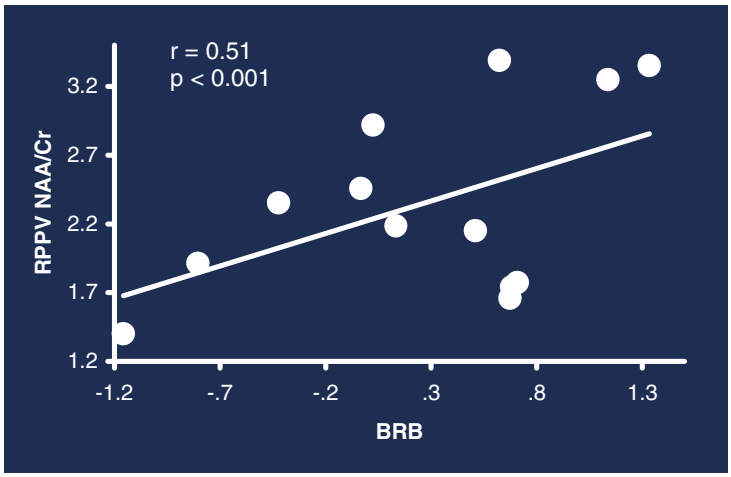

Fig. 9. A positive correlation between right posterior periventricular RPPV NAA/Cr and BRB scores observed in WM

4 Discussion and Conclusions

Mixture-based image segmentation is a theoretical solution to the PV effect and provides the most accurate result in quantifying tissue volumes and textures. Mapping the

low-resolution MRS data onto the segmented high-resolution tissue distribution offers a unique way to study both structural and functional changes of the brain tissues.

Cerebral atrophy and brain metabolite level correlate with each other as well as BRB scores assessed by cognitive functions.

Brain metabolite level measured by ^{1}H MRS can be quantitatively mapped onto segmented tissue mixtures in each image voxel for correlation studies between MRI and MRS.

As both MRI and MRS are spatially registered, a correlation study can be performed both globally and locally across the FOV.

The integrated MRI/MRS framework shall open a new way to explore the MRS metabolic changes and MRI morphological processes for studying brain functions.

Acknowledgements

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